Gene replacement in stem cells made easier

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A press release about CIRM grantees at the Salk Institute for Biological Studies contains what might be the truest words in stem cell science:

> In principle, genetic engineering is simple, but in practice, replacing a faulty gene with a healthy copy is anything but.

Several CIRM grantees could sum up their work in that same way. We've funded a variety of projects that all intend to replace faulty genes in stem cells with healthy ones, and then use the tricked-up stem cells to treat disease. That's how both of our HIV/AIDS disease teams hope to conquer HIV infection and also underlies our sickle cell disease and epidermolysis bullosa teams. (A list of disease teams with links to their research summaries is available here.)

The Salk researchers have published a paper in Cell Stem Cell describing a new way of replacing a gene with a therapeutic version. As a model, they used stem cells they had reprogrammed from a person with a genetic premature aging condition called Hutchinson-Gilford progeria. That condition is caused by a mutation in a gene called Lamin A. They used the technique to replace the defective Lamin A in the reprogrammed stem cells with a healthy copy of the gene. According to postdoctoral researcher and co-first author Guang-Hui Liu:

> "The process was remarkably efficient and we couldn't detect any undesired off-target effects such genomic instability or epigenetic abnormalities," says Liu. "What's more, it allowed us to show that we can correct multiple mutations spanning large genomic regions."

The group also showed that their technique worked in mesenchymal stem cells, which are a form of tissue-specific stem cells many groups are also using to develop therapies.

The issue of being able to swap out defective genes is just one of many hurdles for scientists developing stem cell-based therapies. These behind-the-scenes issues rarely make the newspapers and remain largely invisible to the people who are waiting to see those future therapies, but are an active area of research for CIRM grantees. Hopefully work like this will help eliminate those hurdles and speed the path to the clinic.

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